DOCKET NO.: ISIS-5297 PATENT

Application No.: Not Yet Assigned

Preliminary Amendment - First Action Not Yet Received

This listing of claims will replace all prior versions, and listings, of claims in the application. Listing of Claims:

1-24 canceled.

- 25. (Currently amended) A method for protecting a hydroxyl moiety of a nucleic acid at at least one of a 2'-O, 3'-O, or 5'-O position comprising reacting said nucleic acid with levulinic acid in the presence of a coupling agent that is attached to a polymeric support for a time and under conditions effective to form an ester at said 2'-O, 3'-O or 5'-O position.
- 26. (Original) The method of claim 25 wherein said nucleic acid is a nucleoside.
- 27. (Original) The method of claim 25 wherein said coupling agent is a carbodiimide.
- 28. (Original) The method of claim 25 wherein said carbodiimide is cyclohexylcarbodiimide.
- 29. (Original) The method of claim 25 wherein said polymeric support is a polystyrene.
- 30. (Original) The method of claim 25 wherein said polymeric support is a polyethylene glycol.
- 31. (Original) A method for acylating at least one hydroxyl moiety of a carbohydrate comprising reacting said carbohydrate with levulinic acid in the presence of a coupling agent that is attached to a polymeric support for a time and under conditions effective to form an ester.
- 32. (Original) The method of claim 31 wherein said coupling agent is a carbodiimide.
- 33. (Original) The method of claim 32 wherein said carbodiimide is cyclohexylcarbodiimide.
- 34. (Original) The method of claim 31 wherein said polymeric support is a polystyrene support.
- 35. (Original) The method of claim 31 wherein said polymeric support is a polyethylene glycol support.
- 36. (Original) A method for acylating at least one hydroxyl moiety of a steroid molecule comprising reacting said steroid molecule with levulinic acid in the presence of a coupling

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agent that is attached to a polymeric support for a time and under conditions effective to form an ester.

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37. (Original) The method of claim 36 wherein said coupling agent is a carbodiimide.

38. (Original) The method of claim 37 wherein said carbodiimide is cyclohexylcarbodiimide.

- 39. (Original) The method of claim 36 wherein said polymeric support is a polystyrene support.
- 40. (Original) The method of claim 36 wherein said polymeric support is a polyethylene glycol support.
- 41. (Original) A method for protecting a hydroxyl moiety on a compound having the following formula:

$$T_1$$
 O B_2 T_2 R

wherein:

B_X is a nucleobase;

 T_1 and T_2 , independently, are OH, a hydroxyl protecting group, an activated phosphate group, a nucleotide, a nucleoside, or an oligonucleotide;

R is -H, -hydroxyl, a protected hydroxyl or a 2' substituent group;

provided that at least one of T₁, T₂ or R is -OH;

comprising reacting said compound with levulinic acid in the presence of a coupling agent that is attached to a solid support for a time and under conditions effective to form an ester between said hydroxyl moiety and the levulinyl group.

42. (Original) The method of claim 41 wherein said coupling agent is a carbodiimide.

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43. (Original) The method of claim 42 wherein said carbodiimide is a cyclohexylcarbodiimide.

44. (Original) The method of claim 41 wherein said polymeric support is a polystyrene support.

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- 45. (Original) The method of claim 41 wherein said polymeric support is a polyethyleneglycol support.
- 46. (Original) A method for protecting the 3'-O and 5'-O positions of a compound having the following formula:

wherein:

 B_X is a nucleobase; and

R is -H, or a 2' - substituent;

comprising reacting said compound with levulinic acid in the presence of a coupling agent that is attached to a solid support for a time and under conditions effective to form a compound having formula:

wherein Lev is a -levulinyl.

- 47. (Original) The method of claim 46 wherein said coupling agent attached to a polymeric support is cyclohexylcarbodiimide attached to a polymeric support.
- 48. (Original) The method of claim 47 wherein said polymeric support is a polystyrene polymeric support.

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49. (Original) A method for protecting the 3'-O and 5'-O positions of a compound having the following formula:

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wherein:

B_X is a nucleobase; and

R is –H, or a 2'- substituent;

comprising reacting said compound with levulinic acid in the presence of cyclohexylcarbodiimide that is attached to a polystyrene polymeric support for a time and under conditions effective to form a compound having the following formula:

wherein Lev is -levulinyl.

- 50. (Original) A method for acylating a hydroxyl moiety comprising reacting said hydroxyl moiety with levulinic acid in the presence of a coupling agent that is attached to a polymericic support for a time and under conditions effective to yield an ester.
- 51. (Original) The method of claim 50 wherein said coupling agent is a carbodiimide
- 52. (Original) The method of claim 51 wherein said carbodiimide is cyclohexylcarbodiimide.
- 53. (Original) The method of claim 50 wherein said polymeric support is a polystyrene.
- 54. (Original) The method of claim 50 wherein said polymeric support is polyethylene glycol.

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55. (Original) A method for generating a cyclohexylcarbodiimide derivatized polymeric support from a cyclohexylurea derivatized polymeric support comprising reacting said cyclohexylurea derivatized polymeric support with a dehydrating agent in an organic solvent for a time and under conditions effective to yield said cyclohexylcarbodiimide derivatized polymeric support.

- 56. (Original) The method of claim 55 wherein said dehydrating agent is POCl₃.
- 57. (Original) The method of claim 55 wherein said dehydrating agent is tosylchloride.
- 58. (Original) The method of claim 55 wherein said organic solvent is CH₂Cl₂, CHCl₃, hexane, or pyridine.
- 59. (Original) The method of claim 55 wherein said polymeric support is a polystyrene polymeric support.
- 60. (Original) A method for generating a cyclohexylcarbodiimide derivatized polymeric support from a cyclohexylurea derivatized polymeric support comprising the steps of:

reacting said cyclohexylurea derivatized polymer support with a dehydrating agent in an organic solvent for a time and under conditions effective to form a salt;

contacting said salt with an aqueous solution to form said cyclohexylcarbodiimide derivatized polymeric support.

- 61. (Original) The method of claim 60 wherein said dehydrating agent is POCl₃.
- 62. (Original) The method of claim 60 wherein said dehydrating agent is tosylchloride.
- 63. (Original) The method of claim 60 wherein said organic solvent is CH₂Cl₂, CHCl₃, hexane, or pyridine.
- 64. (Original) The method of claim 60 wherein said polymeric support is a polystyrene polymeric support.